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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/399,083	09/17/99	CALDERWOOD D	BBC-043PA2

HM12/0324

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1624	7

DATE MAILED: 03/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/399,083	Calderwood et al.
Examiner	**Group Art Unit**
Deepak Rao	1624

☒ Responsive to communication(s) filed on *Sep 17, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-45* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-45* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Claims 1-45 are pending in this application.

Note: Claim number 3 was repeated and claim number 8 was missing. Accordingly, as per Rule 1.126, from the second occurrence of no. 3, the claims were renumbered.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e), and the reference to parent application of which the instant application is a CIP, is acknowledged. However, it is observed that the parent application 09/042,702 claimed the benefit of provisional application 60/040,836, filed March 19, 1997. The first paragraph of the specification should be updated with this information.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

On pages 175-214, in many of the structural formulae, the bonds between sulfur and oxygen are not either not present or invisible. Without the double bond (=) between the S and O, the structure appears to be incomplete. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to enable the preparation of the claimed compounds. According to the instant claims, A, R, R', R_2, R_3, R_4, R_5, Z, R_f, R_g, R_c, R_d, R_e, R_i, D etc. are defined to be "substituted" groups such as "aliphatic", "aromatic", heteroaromatic", etc. and no explanation has been provided for the size or nature of these aliphatic/aromatic/heterocyclic... groups. Scope of "substituted" with respect to these groups in the claims read on all functional moieties regardless of complexity of structure, rings having any number of nitrogen, oxygen, sulfur atoms in any array for the recited groups. The schemes in the specification pages 60-70, discloses the essential starting materials to prepare the claimed compounds, however, in the discussion of the sources of the starting materials, there is no disclosure regarding the essential starting materials needed to prepare the instantly claimed compounds having the 'substituted' groups such as 'aliphatic', 'heteroaromatic', etc. Sources of certain starting materials are given in the examples wherein A is a phenyl, however, none to show the representatives of the other groups that are defined for ring

A which are further optionally substituted. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

The specification fails to enable one skilled in the art to use the claimed compounds. The use disclosed in the specification is as inhibitors of protein kinases useful in the treatment of a variety of disease conditions. Testing assays and procedures are provided in pages 53-60, however, none of the instantly claimed compounds have been tested for the claimed activity. Preparation of many of the instantly claimed compounds is not enabled (as explained above) and the exemplified compounds are not considered to be representative of all the possible compounds encompassed by the claims. The exemplified compounds are structurally very different from all the compounds embraced by the instant claims (many of the variables are defined to be 'substituted' groups) such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the instantly claimed compounds. Note *In re Surrey,* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. In view of the breadth of the claims, the chemical nature of the invention, and the lack of working examples regarding the activity of the compounds encompassed by the generic definition of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds as protein kinase inhibitors.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. The various "substituted" groups such as 'substituted aliphatic', 'substituted aromatic', 'substituted heteroaromatic', etc. throughout claims 1-7 is unclear as to the nature and number of substituent(s) intended. Note *In re Wiggins*, 179 USPQ 421 regarding such terminology.

2. Claim 1 is drawn to 'compound and pharmaceutically acceptable salts', therefore, it is not clear if compounds are claimed or a mixture consisting of a compound and the corresponding salt is claimed. Replacing "and" with -- or -- is suggested for compound claims.

3. In claim 9, all the species begin with the term "N**1**-", the significance of the number " **1** " is not understood. The terminal portion of each of the species again contains "-1-benzenesulfonamide" and therefore, it is not clear why '1' is recited twice.

4. Claim 11 recites the limitation "-$NHSO_2R$-" and "-NHC(O)R-" for L in lines 1-2. There is insufficient antecedent basis for this limitation in claim 1 on which claim 11 is dependent. The variable " R " is not a divalent group and therefore, presence of this variable in the above two divalent groups is inconsistent with the definition of L in claim 1.

5. In claims 12, 16 and 39, the term "prodrug" is indefinite because they are neither specified nor would they be apparent to one of ordinary skill in the art. As a result, the metes and bounds of the patent protection desired cannot be determined with a reasonable degree of certainty. The specification does not provide any help.

6. Claim 33 recites the limitation "the condition mediated by protein kinsase activity is atherosclerosis, ..." in lines 1-3. There is insufficient antecedent basis for this limitation in claim 32 on which claim 33 is dependent. Claim 32 recites 'the condition mediated by protein kinase is a cardiovascular condition', thereby claim 32 is limited to 'cardiovascular condition' only. However, claim 33 which is dependent on claim 32, does not further limit claim 32 but recites some additional 'conditions' therefore appears to be improperly referring to claim 32.

The dependent claims included here but not particularly referred to are included in the rejections above because they do not resolve one or more of the issues.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Calderwood et al., U.S. Patent No. 6,001,839 (effective filing date March 19, 1997). The instantly claimed compounds read on the compounds of the reference, see the structural formula I in col. 2 and the corresponding species in col. 7-10. Further, the species claimed in claim 9 (page 223, lines 10-11) is identically disclosed, see e.g., col. 10, lines 9-10.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-8 and 10-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Missbach et al., WO 96/10028. The reference teaches a generic group of compounds which

embraces applicant's instantly claimed compounds. See formula (I) in page 1 wherein R3 is aryl substituted with a variety of substituents which include lower alkanoyl amino, N-lower alkylaminocarbonyl, etc. The compounds are taught to be useful as protein tyrosine kinase inhibitors, see the abstract. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as pharmaceutical therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

2. Claims 1-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calderwood et al., 6,001,839 (effective filing date March 17, 1997). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I in col. 2 wherein R_3 is represented by formula (a) and the species in col. 7-10. The reference discloses species that are The compounds are taught to be useful as pharmaceutical therapeutic agents

having protein kinase inhibition activity, see the entire document. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as pharmaceutical therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-45 are rejected under the judicially created doctrine of double patenting over claims 1-27 of U. S. Patent No. 6,001,839 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The reference patent also claims an invention that is identical to the instantly claimed invention, see formula I in col. 37 and further, the specifically claimed compounds in col. 41-42. Further, the reference claim 24 includes one of the compound that is instantly claimed, see col. 42, lines 32-33, which compound is identical to the compound in instant claim 9, page 223, lines 10-11.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

2. Claims 1-45 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,001,839. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no patentable distinction. While many of the compounds instantly claimed substantially overlap the reference compounds, the others are generically embraced which would have been obvious to one of ordinary skill in the art. One of ordinary skill in the art would have been motivated to

select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole.

Receipt is acknowledged of the Information Disclosure Statement filed on February 23, 2000 and a copy is enclosed herewith.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Rao whose telephone number is (703) 305-1879. The fax phone number for this Group is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Deepak Rao
March 23, 2000

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